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A Case of Multifactorial Orthostatic Hypotension Complicated by Chemotherapy Associated Autonomic Toxicity

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Introduction

Autonomic neuropathy is known to occur as a side effect of some chemotherapy drugs, including cisplatin. This report presents a patient with new onset of autonomic instability and orthostatic hypotension after receiving multiple rounds of cisplatin and gemcitabine chemotherapy.

Section Title

HPI

An 81 year old man with history of stage III lung cancer **presented after a fall at home** that occurred while getting out of bed in the middle of the night

Cancer was treated with lobectomy and lymphadenectomy 5 months prior to his admission, followed by **3 rounds of chemotherapy with cisplatin and gemcitabine**

He was admitted 4 days prior for weakness and back pain, and was empirically started on tamsulosin for urinary retention

Objective

Patient was noted to have remarkable orthostatic hypotension on admission:

BP - HR

Supine: 180/84 - 91

Standing : 89/39 - 121

Initial cardiovascular workup reassuring with normal troponin, EKG. Basic labs were unremarkable except for chronic anemia

Hospital Course

Initially managed with IV fluids which did not resolve his orthostatic hypotension

Discontinued tamsulosin and other medications with risks of falls or hypotension, still with continued symptoms

On the first night after admission, the patient was found to have **dramatically high blood pressures while supine with systolic pressure above 200 mmHg**, indicative of autonomic neuropathy

Managed with compression stockings, abdominal binder, and getting patient up to chair and out of bed as frequently as possible while minimizing time spent supine

On 5th day of admission, the patient was able to ambulate multiple times throughout the day without hypotension, and was discharged home

Orthostatic hypotension recurred on a subsequent admission one month later and the patient was transitioned to hospice care

Figure 1: Autonomic Cardiovascular Axis

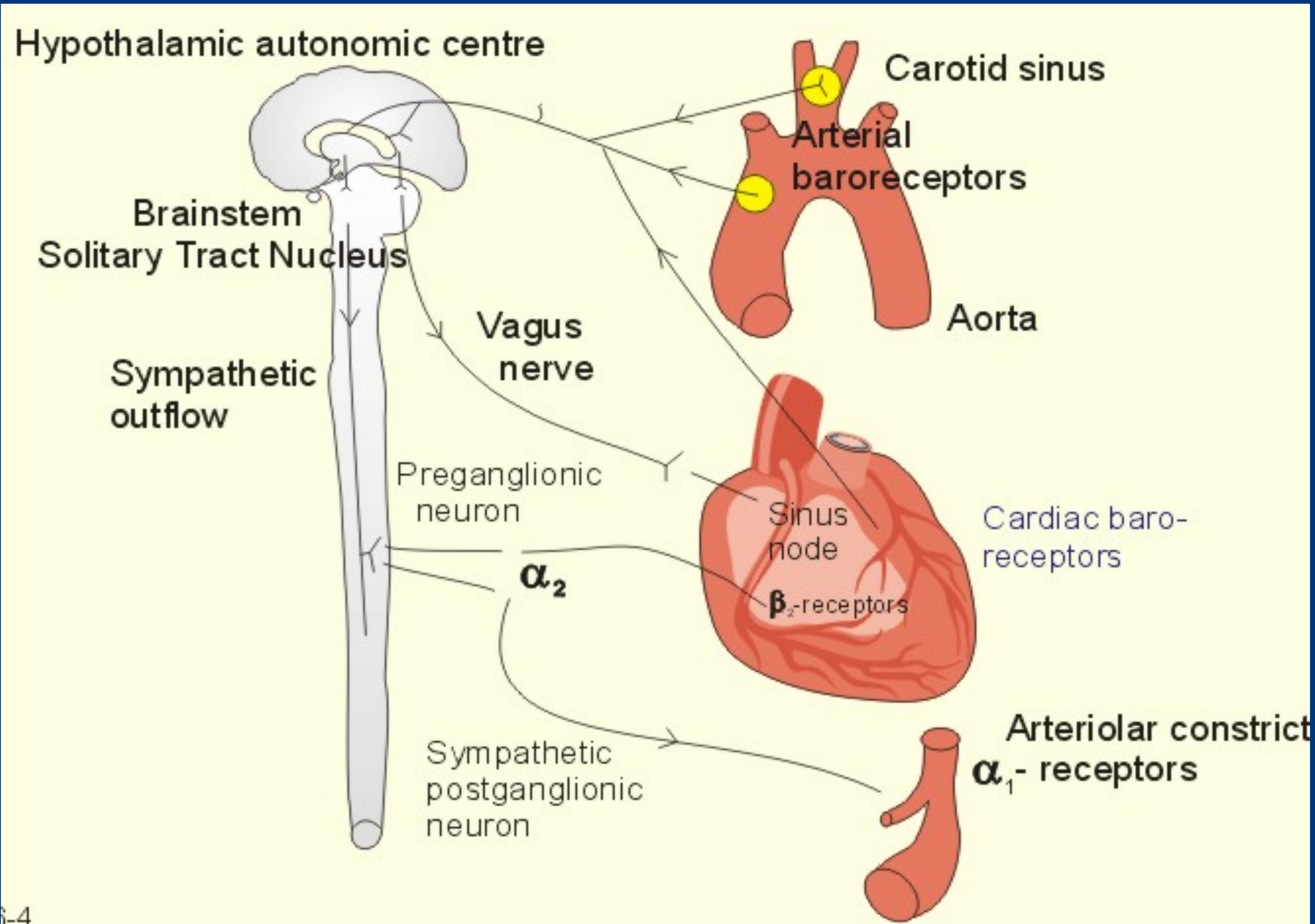
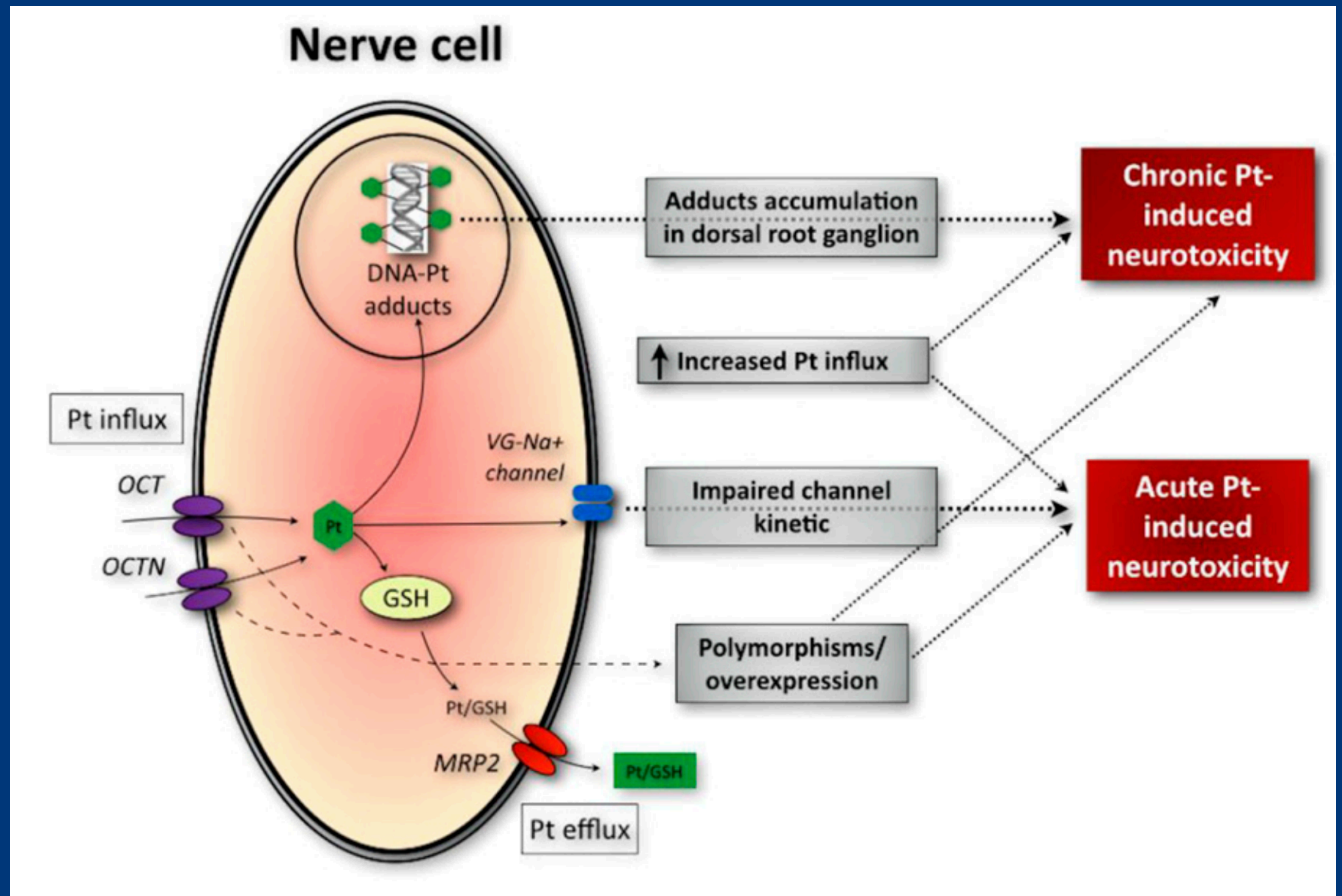


Figure 2: Neurotoxicity of Platinum Based Chemotherapy



Tools for Management of Refractory Orthostatic Hypotension



Figure 3: Abdominal Binder



Figure 4: Compression Stockings

Discussion

Diagnosis of Autonomic Neuropathy

- Hypovolemic and medication associated etiologies were ruled out when symptoms persisted after initial management
- Autonomic dysfunction was suggested by severe supine hypertension, inconsistent heart rate response to hypotension, and recent new onset urinary retention

Chemotherapy-Associated Neuropathy

- While uncommon, a number of case reports^{1,2,3,4} describe autonomic neuropathy in association with cisplatin, which was determined to be the most likely etiology in this case, given the timeline of presentation
- Neurotoxicity from platinum based drugs is speculated to result from progressive DNA-adduct accumulation and inhibition of DNA repair pathways, with resultant apoptosis⁵
- The drug accumulates in peripheral nerves and dorsal root ganglia; while this more commonly results in peripheral neuropathy, individual patient factors including genetic influences on DNA repair and drug transport mechanisms may explain varying toxicity effects

Management of Refractory Orthostatic Hypotension

- Severe hypertension limited the use of pressure support medications such as midodrine or fludrocortisone
- This required creative problem solving including the use of an abdominal binder, compression stockings, and minimizing time spent supine to stabilize the patient for discharge

Takeaways

- Autonomic neuropathy is a rare side effect associated with cisplatin chemotherapy, which can result in orthostatic hypotension; other implicated drugs include paclitaxel, taxanes, and vinca alkaloids
- Key points that indicated an atypical cause of orthostatic hypotension in this case were the lack of response to fluid resuscitation and autonomic instability with high blood pressures while the patient was supine
- When orthostatic hypotension is complicated by autonomic instability with severe hypertension, management may require creative strategies including abdominal binders, compression stockings, physical therapy, and minimizing time spent supine

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